

CLAIMS:

1. A method of identifying modulators of AMPK-mediated activation of a nitric oxide synthase enzyme selected from the group consisting of eNOS, nNOS and nNOS μ , comprising
5 the step of testing putative modulators for their ability to increase or decrease phosphorylation of the enzyme, said increase or decrease depending on the calmodulin and calcium ion concentrations.
2. A method according to claim 1, in which the specific
10 phosphorylation of Ser-1177 is assessed in the presence of calcium and calmodulin.
3. A method of identifying modulators of AMPK-mediated inhibition of eNOS, comprising the step of testing a putative modulator for its ability to decrease or increase
15 AMPK-mediated phosphorylation of eNOS in the presence of limiting calcium ions.
4. A method according to claim 3, in which the specific phosphorylation of Thr-495 is assessed.
5. A method according to any one of Claims 1 to 4, in
20 which one or more of the following activities is additionally assessed:
- (a) Effect on smooth muscle contraction;
 - (b) Effect on inotropic activity of the heart;
 - (c) Effect on chronotropic activity of the heart; or
 - 25 (d) Effect on platelet function.
6. A method according to any one of Claims 1 to 5, in which the modulator is an activator, as herein defined.
7. A method according to Claim 6, in which the activator promotes both glucose metabolism and fatty acid metabolism.

8. A method according to any one of Claims 1 to 5, in which the modulator is an inhibitor, as herein defined.

9. A method according to any one of Claims 3 to 8, in which the modulator acts preferentially on non-neuronal cells.

10. A method according to Claim 1 or Claim 2, in which the modulator promotes the dephosphorylation of Ser-1177 and inhibits eNOS activity.

11. A method according to Claim 3, in which the modulator
10 promotes the dephosphorylation of Thr-495 and stimulates
eNOS activity.

12. A method according to Claim 1 or Claim 2 in which the modulator promotes phosphorylation of nNOS or nNOS μ at Ser-1417.

15 13. A method according to Claim 1 or Claim 2 in which the modulator promotes dephosphorylation of nNOS or nNOS μ at Ser-1417.

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